

FILE 'HCAPLUS' ENTERED AT 16:41:30 ON 24 NOV 2008

L1 68019 S POLYSACCHARIDE  
L2 11051 S (TYPE 5) OR CAPSULAT  
L3 18409 S (TYPE 5) OR CAPSULAR  
L4 3525 S PNEUMOCOCCUS  
L5 4703 S L1 AND (L4 OR L3)  
L6 297 S L1 AND (L4 AND L3)  
L7 250 S L6 AND (PY<2003 OR AY<2003 OR PRY<2003)  
L8 1540559 S MICROWAVE OR PH  
L9 14 S L7 AND L8  
L10 0 S REDUCTINVE AMINATION  
L11 7825 S (REDUCTIVE AMINATION) OR CYANOBOROHYDRIDE  
L12 0 S L7 AND L11  
L13 37 S L1 AND (L3 OR L4) AND L11  
L14 28 S L13 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file hcaplus		
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FILE COVERS 1907 - 24 Nov 2008 VOL 149 ISS 22  
 FILE LAST UPDATED: 23 Nov 2008 (20081123/ED)

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```
=> s polysaccharide
L1      68019 POLYSACCHARIDE

=> s (type 5) or capsulat
      1986819 TYPE
      6857006 5
      11050 TYPE 5
          (TYPE(W)5)
          1 CAPSULAT
L2      11051 (TYPE 5) OR CAPSULAT

=> s (type 5) or capsular
      1986819 TYPE
      6857006 5
      11050 TYPE 5
          (TYPE(W)5)
          7450 CAPSULAR
L3      18409 (TYPE 5) OR CAPSULAR

=> s pneumococcus
L4      3525 PNEUMOCOCCUS

=> s l1 and (L4 or L3)
L5      4703 L1 AND (L4 OR L3)

=> s l1 and (L4 and L3)
L6      297 L1 AND (L4 AND L3)

=> L6 and (PY<2003 or AY<2003 or PRY<2003)
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L6 IS NOT A RECOGNIZED COMMAND

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=> s L6 and (PY<2003 or AY<2003 or PRY<2003)

22961900 PY<2003

4500211 AY<2003

3968587 PRY<2003

L7 250 L6 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> s microwave or pH

134767 MICROWAVE

1408158 PH

L8 1540559 MICROWAVE OR PH

=> s l7 and l8

L9 14 L7 AND L8

=> d l9 1-14 ti abs bib

L9 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis of a conjugate vaccine composed of pneumococcus type  
14 capsular polysaccharide bound to pertussis toxin

AB Type 14 is one of the common types isolated from patients of all ages with  
infections caused by Streptococcus pneumoniae. Its capsular  
polysaccharide (Pn14) is composed of a neutrally charged  
tetrasaccharide repeat unit. Pn14 does not elicit protective levels of  
antibodies in infants and children and is a less than optimal immunogen of  
the 23-valent vaccine for adults. Pertussis toxin (PT) is both a  
virulence factor and protective antigen of Bordetella pertussis: it is not  
soluble at neutral pH and forms insol. complexes with acidic  
polysaccharides. Both Pn14 and PT are potential components of vaccines  
for infants and children. Accordingly, a synthetic scheme was devised to  
prepare a conjugate of Pn14 and PT. An adipic acid hydrazide derivative of

Pn14 was bound to PT at pH 3.9 by carbodiimide-mediated condensation.  
The conjugation procedure inactivated the PT as assayed by CHO cell and  
histamine-sensitizing activity. The Pn14-PT conjugate elicited antibodies  
in mice to Pn14 at levels estimated to be protective in humans and elicited  
neutralizing antibodies to PT.

AN 1993:37207 HCAPLUS <<LOGINID::20081124>>

DN 118:37207

OREF 118:6759a,6762a

TI Synthesis of a conjugate vaccine composed of pneumococcus type  
14 capsular polysaccharide bound to pertussis toxin

AU Schneerson, Rachel; Levi, Lily; Robbins, John B.; Bryla, Dolores M.;  
Schiffman, Gerald; Lagergard, Teresa

CS Lab. Dev. Mol. Immun., Natl. Inst. Child Health Hum. Dev., Bethesda, MD,  
20892, USA

SO Infection and Immunity (1992), 60(9), 3528-32  
CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

L9 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Multivalent pneumococcal vaccine and preparation thereof

AB A multivalent pneumococcal vaccine, comprising immunolog.-active purified  
pneumococcal capsular polysaccharide (substantially  
absent C4 polysaccharide) of the types 1, 2, 3, 4, 5, 6B, 7F, 8,  
9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F

(Danish designation) is prepared using a series of purification steps. Thus, a Pneumococcus type 3 fermentation lysate is precipitated with 0.15-0.5 volume alc.

at pH 6.7 and 2-6°, and redissolved in 4% NaAcO. The process is repeated twice, using 0.25-0.6 and 0.1-0.5 volume alc., resp. Impurities are further removed by fractional precipitation with 0.1-0.5 vol % cetavlon (based on 10% cetavlon solution), at pH 7.4 and 21-25°. The polysaccharide is repptd. at pH 6.7 and 4° with .apprx.4% NaAcO and .apprx.0.5 volume alc., and this step is repeated twice. The polysaccharide is dissolved in pyrogen-free water and the solution is adjusted to pH 6.1 with 0.3M HAcO. NaCl is added to 0.15M concentration and activated charcoal is added to

5% concentration, followed by filtering, dialysis, freezing and lyophilizing, to give an immunogenic product free of proteins and nucleic acids.

AN 1986:49841 HCAPLUS <<LOGINID::20081124>>

DN 104:49841

OREF 104:8033a,8036a

TI Multivalent pneumococcal vaccine and preparation thereof

IN Ritchey, Mary B.; Cano, Francis R.; O'Hara, Gerald J.; English, James D.; Lin, Wenlii

PA American Cyanamid Co. , USA

SO Eur. Pat. Appl., 63 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 157899	A2	19851016	EP 1984-105559	19840516 <--
	EP 157899	A3	19870909		
	EP 157899	B1	19920617		
	R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
	US 4686102	A	19870811	US 1984-599318	19840412 <--
	CA 1216235	A1	19870106	CA 1984-455036	19840524 <--
	JP 60218325	A	19851101	JP 1984-155729	19840727 <--
	JP 06041422	B	19940601		
	AU 8541016	A	19851017	AU 1985-41016	19850411 <--
	AU 569946	B2	19880225		
	ZA 8502724	A	19851127	ZA 1985-2724	19850411 <--
	AT 399655	B	19950626	AT 1985-1090	19850411 <--
PRAI	US 1984-599318	A	19840412	<--	

L9 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Modification of a direct enzyme-linked immunosorbent assay for the detection of immunoglobulin G and M antibodies to pneumococcal capsular polysaccharide

AB In contrast to the usual indirect ELISA method for detection of antibody responses, a modified direct ELISA technique was used to measure IgG and IgM responses to pneumococcal capsular types 1, 3, 9N, and 23F in humans. Individual capsular polysaccharides were covalently bound to poly-L-lysine before adsorption to the solid phase. The coupling reaction was enhanced by maintenance of a constant pH of 8.2 after the addition of all reactants. The evaluation of 4 diluents [phosphate-buffered saline (PBS)-Tween; PBS-Tween plus 10% fetal calf serum; PBS-Tween plus 10% bovine serum albumin; and PBS-Tween plus 20% normal goat serum] showed that the sensitivity and specificity of the assay was increased with normal goat serum (10-fold). Serum samples from subjects immunized with polyvalent pneumococcal vaccine were tested by direct ELISA and by radioimmunoassay. At 4 wk postimmunization, the ELISA method showed that IgG was the predominant antibody and the IgM responses

were lower or had diminished. Isotype shifts during this period would have been undetected by the radioimmunoassay method. The changes in antibody response measured by ELISA were comparable to the radioimmunoassay results. The direct ELISA method for the detection of antipneumococcal capsular antibody is a sensitive and reproducible assay for the detection of IgG and IgM antibodies.

AN 1985:129995 HCAPLUS <<LOGINID::20081124>>

DN 102:129995

OREF 102:20377a,20380a

TI Modification of a direct enzyme-linked immunosorbent assay for the detection of immunoglobulin G and M antibodies to pneumococcal capsular polysaccharide

AU Messina, J. P.; Hickox, P. G.; Lepow, M. L.; Pollara, B.; Venezia, R. A.

CS Albany Med. Coll., Union Univ., Albany, NY, 12208, USA

SO Journal of Clinical Microbiology (1985), 21(3), 390-4

CODEN: JCMIDW; ISSN: 0095-1137

DT Journal

LA English

L9 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Hydrolytic stability of pneumococcal group 6 (type 6A and 6B) capsular polysaccharides

GI For diagram(s), see printed CA Issue.

AB The hydrolyses of the immunol. cross-reactive and constitutionally isomeric group 6 pneumococcal polysaccharides, types 6A and 6B with repeating units I (R = 5-phosphoribos-3-yl and 5-phosphoribos-4-yl) resp., were studied by <sup>31</sup>P NMR spectroscopy, gel filtration through Sepharose 4B, reducing-sugar anal., and rocket immunoelectrophoresis. <sup>31</sup>P NMR spectroscopy showed that cleavage of the repeating-unit phosphodiester linkages at pH 10 and 60° was considerably faster (>103) for the type 6A than the type 6B polysaccharide. <sup>31</sup>P NMR kinetic measurements showed that the Na<sup>+</sup> form of the type 6A polysaccharide underwent phosphodiester-linkage hydrolysis 2-fold slower than the corresponding Ca<sup>2+</sup> form; a stoichiometric excess of Ca<sup>2+</sup> caused a 30-fold enhancement of the rate of hydrolysis of the latter. Heating the polysaccharides at 56° for various times led to a considerably faster decrease in the size of the type 6A antigen than of the type 6B antigen (as measured by gel filtration coeffs. of distribution, K<sub>d</sub> values). The K<sub>d</sub> values for size reduction correlated with the loss of immunochem. reactivity (measured by rocket immunoelectrophoresis). The kinetics of depolymn. of the polysaccharides was consistent with random bond cleavage. The acetal linkages of the type 6A and 6B polysaccharides were comparatively resistant to hydrolysis; depolymn. by hydrolysis of the phosphodiester linkage was a major factor only in the type 6A. Probably, the hydrolytic stability of the type 6B antigen would favor its use in polyvalent pneumococcal vaccine rather than the cross-reactive, but comparatively unstable, type 6A polysaccharide.

AN 1982:508295 HCAPLUS <<LOGINID::20081124>>

DN 97:108295

OREF 97:17998h,17999a

TI Hydrolytic stability of pneumococcal group 6 (type 6A and 6B) capsular polysaccharides

AU Zon, Gerald; Szu, Shousun C.; Egan, William; Robbins, Joan D.; Robbins, John B.

CS Dep. Chem., Cathol. Univ. America, Washington, DC, 20064, USA

SO Infection and Immunity (1982), 37(1), 89-103

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

L9 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Countercurrent immunoelectrophoresis: improved detection of pneumococcal capsular antigens in sputum by incorporation of a carboxylated derivative of phenyl boronic acid

AB Incorporation of m-carboxyphenylboronic acid (mCPB) into a 1% agarose gel support prior to countercurrent electrophoresis with a barbitol buffer increased number of sputum samples registered as pos. for pneumococcal polysaccharide types 7 and 14 by countercurrent immunoelectrophoresis. The most drastic improvement occurred when the electrophoresis was carried out at pH 8.6 and precipitation allowed to occur during overnight refrigeration. The improvement in sensitivity is attributed to improvement in the anodal migration ability of the normally elec. neutral type 7 and 14 capsular polysaccharide by binding with mCPB.

AN 1980:39544 HCAPLUS <<LOGINID::20081124>>

DN 92:39544

OREF 92:6611a,6614a

TI Countercurrent immunoelectrophoresis: improved detection of pneumococcal capsular antigens in sputum by incorporation of a carboxylated derivative of phenyl boronic acid

AU Kelsey, M. C.; Reed, C. S.

CS Dep. Clin. Pathol., Univ. Coll. Hosp., London, WC1E 6AU, UK

SO Journal of Clinical Pathology (1979), 32(9), 960-2  
CODEN: JCPAAK; ISSN: 0021-9746

DT Journal

LA English

L9 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Immunochemical studies on equine immunoglobulins. Part VI. Combining site specificity of antipneumococcal type VIII horse immunoglobulins cross-reactive with mild acid-treated *Xanthomonas campestris* polysaccharide

AB Following mild acid treatment (pH 1.1 for 1 h at 100°), the extracellular polysaccharide of *X. campestris* (NRRL B-1459) acquires a weak cross-reactivity with horse antipneumococcal type VIII (anti-Pn VIII) serum. The interaction of mild acid-treated xanthomonal polysaccharide with anti-Pn VIII was examined by quant. precipitation and hapten inhibition and compared with data similarly obtained for oat glucan. Igs isolated by a cellobiose-strong salt extraction of specific ppts. formed by anti-Pn VIII with xanthomonal antigen, oat glucan, lichenin, and types III and VIII Pn capsular polysaccharides were identified by the use of monospecific anti-equine heavy chain reagents. Various oligosaccharides, including di-, tri-, tetra-, and pentasaccharides of  $\beta$ -(1  $\rightarrow$  4)-linked glucose (G) as well as  $G\beta(1 \rightarrow 3)$   $G\beta(1 \rightarrow 4)G$  and  $G\beta(1 \rightarrow 3) G\beta(1 \rightarrow 4)G$ , were assayed for their ability to inhibit anti-Pn VIII precipitation by xanthomonal antigen. Combining sites of antibody cross-precipitated by xanthomonal antigen optimally accommodate a cellodextrin structure consisting of a terminal or internal sequence of only 2  $\beta$ -(1  $\rightarrow$  4)-linked glucose units. Inhibition data showing an ordering (cellopentaose = cellotetraose > cellotriose > cellobiose) in the relative ability of cellodextrins to inhibit oat glucan precipitation establish that a sequence for 4 consecutive glucose units in  $\beta$ -(1  $\rightarrow$  4) linkage provides the optimal cellodextrin ligand structure accommodated by combining sites of the anti-Pn VIII fraction interacting with oat glucan.

AN 1978:440695 HCAPLUS <<LOGINID::20081124>>

DN 89:40695

OREF 89:6299a,6302a

TI Immunochemical studies on equine immunoglobulins. Part VI. Combining site specificity of antipneumococcal type VIII horse immunoglobulins cross-reactive with mild acid-treated *Xanthomonas campestris*

polysaccharide

AU Allen, Peter Z.  
 CS Dep. Microbiol., Univ. Rochester Sch. Med. Dent., Rochester, NY, USA  
 SO Archives of Biochemistry and Biophysics (1978), 188(2), 376-84  
 CODEN: ABBIA4; ISSN: 0003-9861

DT Journal  
 LA English

L9 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Inducible polysaccharide depolymerases of *Bacillus palustris*  
 AB The preparation, properties, and method of assay are described of depolymerases of capsular polysaccharides of type III and type VIII pneumococci (S3 and S8). Conditions were studied for the induced formation of the depolymerases, D3 and D8, resp., by *B. palustris* N3574. S8 depolymerase (D8) is formed only when its specific substrates ( polysaccharide of type VIII pneumococcus, oxidized cellulose, or their partial degradation products) are present as the sole C source. S3 depolymerase (D3) is produced even in the presence of other energy sources, provided small amts. of type III pneumococcal polysaccharide or its partial hydrolysis products are added to the medium. Despite these striking differences in substrate specificity, in the conditions necessary for their formation, and differences in their immunochem. behavior and stability as proteins, the depolymerases have similar modes of action. Both are endoenzymes, since they rapidly decrease the viscosity of solns. of their homologous substrates with a slow appearance of reducing groups. Studies on a series of oligosaccharides and polysaccharides showed that the 1,4- $\beta$ -linkage, as in cellobiuronic acid, is a necessary although not sufficient condition for optimum induction of S3 and S8 depolymerases. Likewise, only those saccharides containing the 1,4- $\beta$ -glucuronido linkage are attacked by either depolymerase. The 2 enzymes represent distinct proteins with different heat and pH stabilities and antigenic specificities. Both enzymes cleave linkages at random along the corresponding polysaccharide chain rather than from the ends of the chain. In the case of S8 hydrolysis, the final product is a tetrasaccharide tentatively identified as glucose-1,4- $\beta$ -glucose-1,4- $\alpha$ -galactose-1,4- $\alpha$ -glucuronic acid. The hydrolysis products of S3 contain as yet unidentified oligosaccharides with average chain length of 4 hexose units. The isolated products of both enzymes were examined for their inducing activity. Even the final products of D3 hydrolysis of S3, with reducing activity equivalent to an average chain length of only 4 hexose units are as effective as fully polymerized S3 as an inducer although cellobiuronic acid does not induce at all. Moreover, the kinetics of enzyme induction by dialyzed, fully polymerized S3 are unaffected by the addition of a potent neutralizing anti-D3 rabbit serum to cultures of *B. palustris*. Probably the smallest unit capable of inducing maximum D3 or D8 formation is larger than a tetrasaccharide. In the case of D8, cellobiuronic acid has some activity as an inducer but is inferior to partial hydrolysis products of S8 containing several hexose units.

AN 1962:47833 HCAPLUS <<LOGINID::20081124>>  
 DN 56:47833  
 OREF 56:9107h-i,9108a-e

TI Inducible polysaccharide depolymerases of *Bacillus palustris*  
 AU Torriani, Annamaria; Pappenheimer, A. M., Jr.  
 CS Harvard Univ.  
 SO Journal of Biological Chemistry (1962), 237, 3-13  
 CODEN: JBCHA3; ISSN: 0021-9258

DT Journal  
 LA Unavailable

L9 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Biosynthesis of pneumococcal capsular polysaccharides. I.  
 Properties of the system synthesizing type III capsular  
 polysaccharide  
 AB cf. CA 54, 25041c. The enzyme system from type III capsulated pneumococci  
 which catalyzes the formation of the specific polysaccharide  
 from uridine diphosphoglucose and uridine diphosphoglucuronic acid has a  
 pH optimum at 8.35 and a temperature optimum at 32°. Maximum  
 synthesis of S III was obtained in 60 min. and the rate of synthesis was  
 proportional to enzyme concentration. The reaction depends on Mg, and shows  
 optimum activity when one substrate is present at a concentration of 0.33  
 millimolar and the other at 0.5 millimolar. The activity of the enzyme  
 depends on the presence of preformed type III capsular  
 polysaccharide. Ultracentrifugation showed that the S  
 III-synthesizing system is present in the particulate fraction sedimented  
 between 30,000 g and 140,000 g. Less than 10% of the total enzyme  
 activity is found in the supernatant solution and the synthesis of S III  
 polysaccharide is proportional to the amount of particulate material  
 used. At the highest level of particulate material used, the amount of S  
 III synthesized represents complete utilization of the substrates  
 available. Exts. from a noncapsulated type III pneumococcus  
 also synthesize type III capsular polysaccharide from  
 uridine diphosphoglucose and uridine diphosphoglucuronic acid. The  
 synthetic activity of such exts. is less than that of exts. from  
 capsulated cells.  
 AN 1961:138148 HCAPLUS <<LOGINID::20081124>>  
 DN 55:138148  
 OREF 55:26128g-i,26129a  
 TI Biosynthesis of pneumococcal capsular polysaccharides. I.  
 Properties of the system synthesizing type III capsular  
 polysaccharide  
 AU Smith, Evelyn E. B.; Mills, Geo. T.; Bernheimer, Harriet P.  
 CS State Univ. of New York Coll. of Med., Brooklyn  
 SO Journal of Biological Chemistry (1961), 236, 2179-82  
 CODEN: JBCHA3; ISSN: 0021-9258  
 DT Journal  
 LA Unavailable  
 L9 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN  
 TI Synthesis of type III pneumococcal polysaccharide by suspensions  
 of resting cells  
 AB The capsular polysaccharide (SIII) of type III  
 pneumococci was removed by the SIII enzyme prepared by a method similar to  
 that of Dubos (C.A. 29, 6919.4) and the cells thus deprived of preformed  
 SIII were washed and examined for capacity to synthesize SIII anew. The  
 washed, decapsulated cocci lost their capacity to be agglutinated in  
 type-specific antiserum but again became agglutinable and formed readily  
 measurable amts. of SIII after suspension in a solution containing only glucose  
 and salts. Maximum SIII synthesis required glucose, Mg, K, P, and O. Other  
 fermentable sugars could be substituted for glucose but the yield of SIII  
 was reduced. Synthesis of SIII occurred anaerobically but was increased  
 four- to five-fold by oxygenation of the suspension. The effects of  
 pH and of enzyme poisons, HgCl<sub>2</sub>, iodoacetate, dinitrophenol, HCN,  
 F, azide, arsenite, and malonate on the capacity to form SIII are  
 described.  
 AN 1953:62402 HCAPLUS <<LOGINID::20081124>>  
 DN 47:62402  
 OREF 47:10616a-d  
 TI Synthesis of type III pneumococcal polysaccharide by suspensions  
 of resting cells  
 AU Bernheimer, Alan W.  
 CS New York Univ., New York, NY



SO Journal of Experimental Medicine (1953), 97, 591-600  
CODEN: JEMEAV; ISSN: 0022-1007  
DT Journal  
LA Unavailable

L9 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN  
TI A new method for production of nonspecific capsular swelling of  
the pneumococcus  
AB Pneumococcal polysaccharides appear to combine with various proteins at  
pH 4 to form insol. aggregates. The reaction is reversed by  
readjusting the pH to 7. Nonspecific capsular  
swelling of pneumococci can be produced by many different proteins under  
such conditions, provided the mixture at pH 4 is relatively  
salt-free. It appears that an altered state of the capsular gel  
is produced by interaction of protein and carbohydrate, and in the absence  
of ionized salts the polysaccharide-protein complex becomes more  
hydrophilic and therefore swells.

AN 1948:15902 HCAPLUS <<LOGINID::20081124>>

DN 42:15902

OREF 42:3455d-e

TI A new method for production of nonspecific capsular swelling of  
the pneumococcus

AU Jacox, Ralph F.

CS Univ. of Rochester, NY

SO Proceedings of the Society for Experimental Biology and Medicine (  
1947), 66, 635-8

CODEN: PSEBAA; ISSN: 0037-9727

DT Journal

LA Unavailable

L9 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI The detectability of pneumococcal capsular  
polysaccharide in urine: influence of variation in pH

AB In an extension of previous studies (C. A. 34, 792.9) the influence of  
pH (6-8) on the detectability, by use of appropriate antisera,  
of pneumococcal capsular polysaccharide (I) in normal  
urine was determined for types 1 to 5 and 7, 8 and 14. In all expts. lower  
concns. of I were detected at pH 7-8 than at 6; adjustment of  
urines to be tested to the higher pH was recommended.

AN 1941:9313 HCAPLUS <<LOGINID::20081124>>

DN 35:9313

OREF 35:1507h-i

TI The detectability of pneumococcal capsular  
polysaccharide in urine: influence of variation in pH

AU De Gara, Paul F.; Bukantz, Samuel C.

SO Journal of Immunology (1940), 39, 297-305

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA Unavailable

L9 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Behavior of acid-treated antipneumococcal rabbit antibodies

AB Solns. of pneumococcal rabbit antibody of various types (types 1, 2, 3, 5,  
7, 8, and 14) were acidified to various pH (4.4 to 2.7) with  
lactic, hydrochloric or sulfuric acids. The nature of the acid was found  
to be of no importance. The ppts. obtained were removed and were always  
found to contain no antibody. The acidified antibody solns. were  
neutralized, and dialyzed against 0.85% NaCl for 48 hrs. Antibody solns.  
treated as described showed an increase in the N precipitable by specific  
polysaccharide (up to 50%), and a shift in the antigen-antibody  
combining ratio occurred at the same time; the ratio of mouse-protective

value/N specifically precipitated was lowered. The complement-fixing quality was

impaired or lost when this last ratio was lowered. Loss of complement-fixing quality was also observed with antibody refined by partial peptic digestion; these serums also had low mouse-protective values. The properties of causing capsular swelling and of eliciting passive anaphylactic shock were unimpaired in acid-treated serums. The implications of the observations are discussed. The use of substituted naphthalenesulfonic acids for purification of pneumococcal antibodies is described. Such purified antibody solns. responded similarly to acid treatment.

AN 1940:3252 HCAPLUS <<LOGINID::20081124>>

DN 34:3252

OREF 34:513e-h

TI Behavior of acid-treated antipneumococcal rabbit antibodies

AU Weil, A. J.; Moos, A. M.; Clapp, Frances L.

SO Journal of Immunology (1939), 37, 413-24

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA Unavailable

L9 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Capsular polysaccharide of the type XIV pneumococcus and its relation to the specific substances in the blood

AB Type XIV pneumococci from a human strain were grown on meat infusion broth and collected in a centrifuge. The organisms from 50 l. were resuspended in saline and allowed to autolyze at 37.5° for 72 hrs. The Gram-neg. bacterial detritus was removed by centrifugation and the clear supernatant liquid concentrated in vacuo to 500 cc. Protein was removed by adjusting the pH to 3.78 and centrifuging. The sp. polysaccharide (I) was precipitated by the addition of 1.5 vols. EtOH and purified by repeated solution and repptn. I is soluble in water to approx. 1%. Tests for uronic acids and protein were neg. I is not precipitated or only partially precipitated by heavy metals but is precipitated by tannic acid.

Biuret,

ninhydrin, sulfosalicylic acid, Hopkins-Cole, Millon and xanthoproteic tests were neg. Molisch and amino sugar tests were strong. Analysis of I shows C 44.4, H 6.8, N 5, Ac 9.0, reducing sugar (calculated as glucose) 74, amino sugar 62% and  $[\alpha]_D^{25}$  12.5°. Serologically, I reacts with type XIV antipneumococcal horse and rabbit serums in dilns. as high as 1:4,000,000. It is neither identical nor contaminated with the blood group A substance. I in its natural state, as a part of the intact cell, may well possess sufficient chemical and immunological relationship to the blood group specific substances to incite in the horse the formation of agglutinins for human erythrocytes, simultaneously with the production of other type-specific antibodies. The relationship of I to the blood group specific substances is further substantiated by the fact that absorption of type XIV antipneumococcal horse serum with homologous polysaccharide removes the hemagglutinins for all blood groups. The blood group A specific substance gives a vigorous precipitin reaction in the cold with type XIV antipneumococcus horse (but not with rabbit) serum.

AN 1938:60239 HCAPLUS <<LOGINID::20081124>>

DN 32:60239

OREF 32:8469i,8470a-e

TI Capsular polysaccharide of the type XIV pneumococcus and its relation to the specific substances in the blood

AU Hoagland, Charles L.; Beeson, Paul B.; Goebel, Walther F.

SO Science (Washington, DC, United States) (1938), 88, 261-3

CODEN: SCIEAS; ISSN: 0036-8075

DT Journal  
LA Unavailable

L9 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Decomposition of the capsular polysaccharide of  
pneumococcus type III by a bacterial enzyme

AB An organism (I) has been isolated from peat soil which decomp. the sp.  
capsular polysaccharide (II) of type III  
pneumococcus. The isolation has been made possible by the use of  
a synthetic mineral medium containing the II as sole source of C; by repeated  
transfers in this medium the potential capacity of the I to decompose the  
sp. substance has been progressively increased. I is a pleomorphic  
bacillus, motile and spore forming, exhibiting metachromatic granules; its  
reaction to the Gram stain varies according to the medium on which it is  
grown. It is strictly aerobic and grows well in plain broth and peptone  
solns.; it does not produce gas in any media and forms small amts. of  
acids only on dextrin, galactose, lactose, salicin and trehalose; its  
growth is inhibited by glucose. I decomp. II aerobically, between  
pH 6.2 and 7.8 at room temperature and at 37.5° but not at  
54°. The decomposition of II is inhibited by the presence in the medium  
of other nutrients such as peptones, which act as more readily available  
sources of energy. The action of I is sp.; it does not attack the soluble  
sp. substance of Type I or II pneumococcus nor any of the other  
bacterial polysaccharides thus far tested. I possesses an endocellular  
enzyme; this enzyme has been extracted by autolysis of the bacterial cells; in  
sterile solution it exhibits the same sp. action as do the organisms from  
which it is derived, decomposing only the II. I decomp. II under anaerobic  
as well as aerobic conditions; it is inactivated at 60-65°; the  
rate of decomposition of II is not affected by the presence of normal serum.  
There exists a quant. relationship between the total amount of sp. substance  
decomposed and the amount of enzyme preparation used; the existence of this  
relation makes it possible to express the activity of a given enzyme  
preparation in terms of the minimal amount required for the complete

decomposition of

a given amount of sp. substance. The sp. decomposition of II, by the organism  
as

well as by the I it produces, illustrates once more the specificity of the  
types of pneumococcus and confirms the fact that the  
capsular polysaccharides and not some impurities carried along  
with them are responsible for type specificity.

AN 1931:40437 HCAPLUS <<LOGINID::20081124>>

DN 25:40437

OREF 25:4575b-f

TI Decomposition of the capsular polysaccharide of  
pneumococcus type III by a bacterial enzyme

AU Dubos, Rene; Avery, Oswald T.

SO Journal of Experimental Medicine (1931), 54, 51-71  
CODEN: JEMEAV; ISSN: 0022-1007

DT Journal  
LA Unavailable

=> d his

(FILE 'HOME' ENTERED AT 16:41:18 ON 24 NOV 2008)

FILE 'HCAPLUS' ENTERED AT 16:41:30 ON 24 NOV 2008

L1 68019 S POLYSACCHARIDE  
L2 11051 S (TYPE 5) OR CAPSULAT  
L3 18409 S (TYPE 5) OR CAPSULAR

```

L4          3525 S PNEUMOCOCCUS
L5          4703 S L1 AND (L4 OR L3)
L6          297 S L1 AND (L4 AND L3)
L7          250 S L6 AND (PY<2003 OR AY<2003 OR PRY<2003)
L8          1540559 S MICROWAVE OR PH
L9          14 S L7 AND L8

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=> log hold

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	48.81	49.02
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-11.20	-11.20

SESSION WILL BE HELD FOR 120 MINUTES  
STN INTERNATIONAL SESSION SUSPENDED AT 16:43:25 ON 24 NOV 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \*  
SESSION RESUMED IN FILE 'HCAPLUS' AT 16:51:45 ON 24 NOV 2008  
FILE 'HCAPLUS' ENTERED AT 16:51:45 ON 24 NOV 2008  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)s

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	48.81	49.02
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-11.20	-11.20

```

=> s reductinve amination
      0 REDUCTINVE
      33490 AMINATION
L10      0 REDUCTINVE AMINATION
          (REDUCTINVE(W)AMINATION)

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```

=> s (reductive amination) or cyanoborohydride
      67405 REDUCTIVE
      33490 AMINATION
      6230 REDUCTIVE AMINATION
          (REDUCTIVE(W)AMINATION)
      1870 CYANOBOROHYDRIDE
L11      7825 (REDUCTIVE AMINATION) OR CYANOBOROHYDRIDE

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=> s 17 and 111
L12      0 L7 AND L11

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=> s 11 and (L3 or L4) and L11

L13 37 L1 AND (L3 OR L4) AND L11

=> s l13 and (PY<2003 or AY<2003 or PRY<2003)

22961900 PY<2003

4500211 AY<2003

3968587 PRY<2003

L14 28 L13 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l14 1-28 ti abs bib

L14 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Modified saccharides and their protein conjugates

AB Saccharide-protein conjugates having a new type of linker are described. The conjugates comprising the new linker are prepared from modified capsular saccharides. The linker is especially useful for preparing conjugates of *Neisseria meningitidis* serogroup A saccharide. Conjugates having this new linker have improved immunogenicity compared to other types of conjugates. A process for modifying a capsular saccharide comprises the steps of: (a) providing a capsular saccharide having a hydroxy group; (b) reacting the hydroxy group with a bifunctional reagent, e.g., 1,1'-carbonyldiimidazole or carbonyldi-1,2,4-triazole in an organic solvent; and (c) reacting the product of step (b) with an amino compound, such as 1-amino-4,5-pentanediol. The product of step (c) is cleaved with periodate, thereby providing an aldehyde compound suitable for linking to a protein by a reductive amination reaction using NaBH<sub>3</sub>CN. A pharmaceutical composition comprising a saccharide-protein conjugate, an adjuvant, and a carrier for preventing or treating diseases, such as bacterial meningitis, is also described.

AN 2004:203711 HCAPLUS <<LOGINID::20081124>>

DN 140:240996

TI Modified saccharides and their protein conjugates

IN Giannozzi, Aldo; Averani, Giovanni; Norelli, Francesco; Costantino, Paolo

PA Chiron S.r.l., Italy

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004019992	A1	20040311	WO 2003-IB4194	20030901 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU 2003260921	B2	20080306		
	EP 1534342	A1	20050601	EP 2003-791149	20030901 <--
	EP 1534342	B1	20060308		
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	CN 1688343	A	20051026	CN 2003-823724	20030901 <--
	BR 2003014089	A	20051116	BR 2003-14089	20030901 <--

AT 319481	T	20060315	AT 2003-791149	20030901 <--
JP 2006511465	T	20060406	JP 2004-532625	20030901 <--
NZ 538703	A	20060929	NZ 2003-538703	20030901 <--
ES 2260682	T3	20061101	ES 2003-791149	20030901 <--
MX 2005PA02315	A	20050608	MX 2005-PA2315	20050228 <--
US 20060263390	A1	20061123	US 2005-526124	20050228 <--
PRAI GB 2002-20198	A	20020830	<--	
WO 2003-IB4194	W	20030901		

RE.CNT 3        THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Preclinical evaluation of group B streptococcal polysaccharide conjugate vaccines prepared with a modified diphtheria toxin and a recombinant duck hepatitis B core antigen

AB An effective vaccine against group B streptococcal (GBS) disease will undoubtedly include capsular polysaccharides (CPSs) from each of the five serotypes prevalent in the United States individually coupled to immunogenic proteins. This formulation may require the use of two or more different protein carriers. We preclinically examined the potential of two proteins to serve as effective carriers for GBS type III CPS. Recombinant duck hepatitis B core antigen (rdHBcAg), a particulate protein of viral origin, and a newly mutated form of diphtheria toxin (DTm) were covalently and directly coupled to purified type III CPS by reductive amination. Seventy-seven of 79 (97%) newborn pups born to mouse dams actively vaccinated with type III CPS-rdHBcAg conjugate survived GBS type III challenge, whereas none of the pups born to dams that received an uncoupled mixture of type III CPS and rdHBcAg or saline survived. Likewise, 64 (98%) of 65 pups born to dams vaccinated with type III CPS-DTm conjugate survived challenge, in sharp contrast to no survivors among the pups born to dams vaccinated with an uncoupled mixture of type III CPS and DTm. The presence of type III CPS-specific IgG in serum from dams correlated with pup survival in groups that received a conjugate vaccine, and this serum was opsonically active in vitro against GBS type III. In addition, carrier-specific IgG was also measured in serum from vaccinated mice. These data suggest that the rdHBcAg and DTm may be effective carriers for GBS CPSs.

AN 2001:771468 HCAPLUS <<LOGINID::20081124>>  
 DN 136:384559

TI Preclinical evaluation of group B streptococcal polysaccharide conjugate vaccines prepared with a modified diphtheria toxin and a recombinant duck hepatitis B core antigen

AU Paoletti, Lawrence C.; Peterson, Darrell L.; Legmann, Rachel; Collier, R. John

CS Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Boston, MA, 02115, USA

SO Vaccine (2001), 20(3-4), 370-376  
 CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 30        THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Formulation and characterization of Bordetella pertussis fimbriae as novel carrier proteins for Hib conjugate vaccines

AB Haemophilus influenzae type b (Hib) capsular polysaccharide (polyribosylribitol phosphate, PRP) is the active component of conjugate vaccines that have proven successful in preventing invasive Hib disease. Conjugation of PRP to a protein carrier greatly

improves its immunogenicity providing protection in infants and subsequent antibody maturation upon boosting. In this study, fimbriae isolated from *Bordetella pertussis* have been assessed as novel carrier proteins. These proteins are components of some acellular pertussis vaccines and clinical trials have indicated that fimbriae could be important protective antigens against whooping cough. Fimbriae (Fim2 and Fim3) purified from *B. pertussis* were dissociated in 6 M guanidine hydrochloride, pH 10.5, to produce proteins of defined size and to facilitate the production and characterization of the conjugates. Both carbodiimide-mediated coupling and reductive amination were used to conjugate PRP to dissociated fimbriae. Efficiency of conjugation was determined by size

exclusion

chromatog. followed by protein and polysaccharide anal. of fractionated components. Immunization of rabbits with dissociated fimbriae-PRP conjugates (D.fim-PRP) produced high anti-fimbrial and anti-PRP IgG titers. Use of a D.fim-PRP conjugate could protect against Hib disease and may also augment protection against *B. pertussis*.

AN 2001:334007 HCAPLUS <<LOGINID::20081124>>

DN 136:221575

TI Formulation and characterization of *Bordetella pertussis* fimbriae as novel carrier proteins for Hib conjugate vaccines

AU Crowley-Luke, A.; Reddin, K.; Gorringe, A.; Hudson, M. J.; Robinson, A.

CS Centre for Applied Microbiology and Research, Salisbury, SP4 0JG, UK

SO Vaccine (2001), 19(25-26), 3399-3407

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Novel meningococcal semi-synthetic polysaccharide-protein conjugate vaccines

AB The success of capsular polysaccharide vaccines in adults and particularly in children remains very limited. These thymus independent (TI) antigens are generally not effective in infants. Covalent bonding of these carbohydrate antigens to thymus dependent (TD) proteins can transform them into TD antigens. *Haemophilus influenzae* type b (Hib) conjugate vaccines to prevent meningitis have been the first of these semi-synthetic vaccines to be licensed. Three meningococcal C conjugates to prevent meningitis have been licensed in the U.K., and a pneumococcal conjugate to prevent invasive pneumonia in infants is now licensed in the U.S. Novel procedures have been developed for the preparation of the carbohydrate antigens to be conjugated, as well as selective chemical manipulations of the polysaccharides and efficient coupling chemistries like reductive amination. In addition, alternative carrier proteins, using recombinant technologies, have been utilized to overcome potential overloading of the immune system with conventional carriers, thereby providing better and safer immunogens. Using state of the art modern technologies, a better understanding of the chemical nature of the protective epitopes on the polysaccharide has provided elements for a rational design of these conjugate mols. As a result, following chemical manipulation of the meningococcal C polysaccharide through its de-O-acetylation, new protective epitopes were created that contributed to the superior immunogenicity of NeisVac-C- in clinical trials. For group B meningococci, newly defined conformational protective epitopes, with the N-propionylation of the polysaccharide and the introduction of a new carrier protein (rPorB) as an immunomodulator, resulted in a novel vaccine candidate to prevent meningococcal B disease. The success of these conjugate vaccines will certainly continue to rise

with a better understanding of this new field, which has now become a real technol. platform.

AN 2001:197351 HCAPLUS <<LOGINID::20081124>>

TI Novel meningococcal semi-synthetic polysaccharide-protein conjugate vaccines

AU Michon, Francis; Blake, Milan S.; Fusco, Peter C.

CS Baxter Healthcare Corporation, Columbia, MD, 21046, USA

SO Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) BIOT-044  
CODEN: 69FZD4

PB American Chemical Society

DT Journal; Meeting Abstract

LA English

L14 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Group B Streptococcus capsular polysaccharide-cholera toxin B subunit conjugate vaccines prepared by different methods for intranasal immunization

AB Group B Streptococcus (GBS) type III capsular polysaccharide (CPS III) was conjugated to recombinant cholera toxin B subunit (rCTB) using 3 different methods which employed (1) cystamine and N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), (2) carbodiimide with adipic acid dihydrazide (ADH) as a spacer, or (3) reductive amination (RA). The CPS III-rCTB conjugates were divided into large- and small-mol.-weight (Mr) fractions, and the immunogenicities of the different preps. after intranasal (i.n.) immunization were studied in mice. Both large- and small-Mr conjugates of CPS III-rCTBRA or CPS III-rCTBADH induced high, almost comparable levels of CPS-specific IgG in serum, lungs, and vagina that were generally superior to those obtained with CPS III-rCTBSPDP conjugates or a CPS III and rCTB mixture. However, the smaller-Mr conjugates of CPS III-rCTBRA or CPS III-rCTBADH in most cases elicited a lower anti-CPS IgA immune response than the large-Mr conjugates, and the highest anti-CPS IgA titers in both tissues and serum were obtained with the large-Mr CPS III-rCTBRA conjugate. Serum IgG anti-CPS titers induced by the CPS III-rCTBRA conjugate had high levels of specific IgG1, IgG2a, IgG2b, and IgG3 antibodies. Based on the effectiveness of RA for coupling CPS III to rCTB, RA was also tested for conjugating GBS CPS Ia with rCTB. As for the CPS III-rCTB conjugates, the immunogenicity of CPS Ia was greatly increased by conjugation to rCTB. Intranasal immunization with a combination of CPS Ia-rCTB and CPS III-rCTB conjugates was shown to induce anti-CPS Ia and III immune responses in serum and lungs that were fully comparable with the responses to immunization with the monovalent CPS Ia-rCTB or CPS III-rCTB conjugates. Thus, the GBS CPS III-rCTB and CPS Ia-rCTB conjugates prepared by the RA method may be used in bivalent and possibly also in multivalent mucosal GBS conjugate vaccines.

AN 2001:20258 HCAPLUS <<LOGINID::20081124>>

DN 134:177010

TI Group B Streptococcus capsular polysaccharide-cholera toxin B subunit conjugate vaccines prepared by different methods for intranasal immunization

AU Shen, Xuzhuang; Lagergard, Teresa; Yang, Yonghong; Lindblad, Marianne; Fredriksson, Margareta; Holmgren, Jan

CS Department of Medical Microbiology and Immunology, Goteborg University, Goteborg, S-413 46, Swed.

SO Infection and Immunity (2001), 69(1), 297-306  
CODEN: INFIBR; ISSN: 0019-9567

PB American Society for Microbiology

DT Journal

LA English

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD



ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L14 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN
- TI Preparation and preclinical evaluation of experimental group B streptococcus type III polysaccharide-cholera toxin B subunit conjugate vaccine for intranasal immunization
- AB Streptococcus group B (GBS) is usually carried asymptotically in the vaginal tract of women and can be transferred to the newborn during parturition. Serum antibodies to the capsular polysaccharide (CPS) can prevent invasive diseases, whereas immunity acting at the mucosal surface may be more important to inhibit the mucosal colonization of GBS and thus the risk of infection for the newborn. We prepared different GBS type III CPS-protein conjugate vaccines and evaluated their systemic and mucosal immunogenicity in mice. GBS type III CPS was conjugated to tetanus toxoid (TT) or recombinant cholera toxin B subunit (rCTB) either directly or to rCTB indirectly via TT. The conjugation was performed by different methods: (1) CPS was coupled to TT with 1-ethyl-3 (3-dimethylaminopropyl)-carbodiimide (EDAC), using adipic acid dihydrazide (ADH) as a spacer; (2) CPS was conjugated with rCTB using reductive amination; or, (3) N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) was used to bind rCTB to the TT of the CPS-TT conjugate. Mice were immunized with these conjugates or purified CPS by s.c. and intranasal (i.n.) routes. Antibodies to GBS III in serum, lungs and vagina were measured with ELISA. All of the CPS-protein conjugates were superior to unconjugated CPS in eliciting CPS-specific immune responses in serum and mucosal tissue exts. The conjugates, when administered s.c., induced only IgG responses in serum, lung and vagina, while i.n. vaccination also elicited IgA responses in the lungs and vagina. The CPS-TT conjugate administered i.n. induced a strong serum IgG, but only a weak mucosal IgA response, while the CPS-rCTB conjugate elicited high IgG as well as IgA antibodies in the lungs after i.n. immunization. GBS III CPS-TT conjugated with rCTB produced a strong systemic and local anti-CPSIII response after i.n. administration. Co-administration of CT as adjuvant enhanced the anti-CPS systemic and mucosal immune responses further after i.n. administration with the CPS conjugates. These findings indicate that: (i) i.n. immunization with GBS CPS-protein conjugates was more effective than s.c. immunization for stimulating serum as well as mucosal immune responses; (ii) rCTB as a carrier protein for GBS III CPS could markedly improve the mucosal immune response; and (iii) the exptl. GBS type III CPS conjugates containing rCTB should be investigated as mucosal vaccine to prevent GBS infection in humans.
- AN 2000:874738 HCAPLUS <<LOGINID::20081124>>
- DN 135:136084
- TI Preparation and preclinical evaluation of experimental group B streptococcus type III polysaccharide-cholera toxin B subunit conjugate vaccine for intranasal immunization
- AU Shen, X.; Lagergard, T.; Yang, Y.; Lindblad, M.; Fredriksson, M.; Holmgren, J.
- CS Department of Medical Microbiology and Immunology, Goteborg University, Goteborg, S-413 46, Swed.
- SO Vaccine (2000), 19(7-8), 850-861  
CODEN: VACCDE; ISSN: 0264-410X
- PB Elsevier Science Ltd.
- DT Journal
- LA English
- RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L14 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN
- TI Use of capsular polysaccharide-tetanus toxoid

conjugate vaccine for type II group B Streptococcus in healthy women  
AB An estimated 15% of invasive group B streptococcal (GBS) disease is caused by  
type II capsular polysaccharide (II CPS). In  
developing a pentavalent vaccine for the prevention of GBS infections,  
individual GBS CPSs have been coupled to tetanus toxoid (TT) to prepare  
vaccines with enhanced immunogenicity. Type II GBS (GBS II) vaccine was  
created by direct, covalent coupling of II CPS to TT by reductive  
amination. In 2 clin. trials, 75 healthy nonpregnant women 18-45  
yr old were randomized to receive II CPS-TT (II-TT) conjugate (dose range,  
3.6-57 µg of CPS component) or uncoupled II CPS vaccine. Both vaccines  
were well tolerated. II CPS-specific IgG serum concns. (as well as IgM  
and IgA) peaked 2 wk after immunization, being higher in recipients of  
conjugated vaccine than in recipients of uncoupled CPS. Immunol.  
responses to conjugate were dose dependent and correlated with  
opsonophagocytosis in vitro. These results support inclusion of II-TT  
conjugate when preparing a multivalent GBS vaccine.

AN 2000:738304 HCAPLUS <<LOGINID::20081124>>

DN 134:279231

TI Use of capsular polysaccharide-tetanus toxoid  
conjugate vaccine for type II group B Streptococcus in healthy women

AU Baker, Carol J.; Paoletti, Lawrence C.; Rench, Marcia A.; Guttormsen,  
Hilde-Kari; Carey, Vincent J.; Hickman, Melissa E.; Kasper, Dennis L.

CS Section of Infectious Diseases, Departments of Pediatrics and Molecular  
Virology and Microbiology, Baylor College of Medicine, Houston, TX, 77030,  
USA

SO Journal of Infectious Diseases (2000), 182(4), 1129-1138

CODEN: JIDIAQ; ISSN: 0022-1899

PB University of Chicago Press

DT Journal

LA English

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Group B streptococcal carbohydrates: Their role in virulence and as  
vaccines.

AB Group B Streptococcus (GBS) is a major cause of neonatal disease in the  
United States. GBS express two distinct surface sugars: the group B  
carbohydrate and the type -specific capsular  
polysaccharide (CPS). Although the former is common to all GBS,  
protective antibody targets predominately the CPS antigen. Of the nine  
structurally and antigenically unique GBS serotypes, five (Ia, Ib, II, and  
V) are prevalent in the U.S. Population. The CPSs of these serotypes are  
comprised of oligosaccharide repeating units containing glucose, galactose,  
N-acetylglucosamine, and N-acetylneuraminic acid. The immunogenicity of  
these otherwise weak antigens has been improved by coupling them directly  
to carrier proteins by reductive amination. GBS  
CPS-protein conjugate vaccines elicit in humans high levels of  
functionally active and protective antibody. An understanding of the  
chemical, biol. and immunol. of GBS CPS antigens has yielded a new generation  
of vaccines against GBS disease.

AN 1999:539754 HCAPLUS <<LOGINID::20081124>>

TI Group B streptococcal carbohydrates: Their role in virulence and as  
vaccines.

AU Paoletti, Lawrence, C.

CS Department of Medicine, Channing Laboratory, Harvard Medical School,  
Boston, MA, 02115, USA

SO Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (  
1999), CARB-021 Publisher: American Chemical Society, Washington,  
D. C.

CODEN: 67ZJA5

DT Conference; Meeting Abstract  
LA English

L14 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Alpha C protein as a carrier for type III capsular polysaccharide and as a protective protein in group B streptococcal vaccines

AB The alpha C protein, a protective surface protein of group B streptococci (GBS), is present in most non-type III GBS strains. Conjugate vaccines composed of the alpha C protein and type III capsular polysaccharide (CPS) might be protective against most GBS infections. In this study, the type III CPS was covalently coupled to full-length, nine-repeat alpha C protein (resulting in III- $\alpha$ 9r conjugate vaccine) or to two-repeat alpha C protein (resulting in III- $\alpha$ 2r conjugate vaccine) by reductive amination. Initial expts. with the III- $\alpha$ 9r vaccine showed that it was poorly immunogenic in mice with respect to both vaccine antigens and was suboptimally efficacious in providing protection in mice against challenge with GBS. Therefore, modified vaccination protocols were used with the III- $\alpha$ 2r vaccine. Female mice were immunized three times with 0.5, 5, or 20  $\mu$ g of the III- $\alpha$ 2r vaccine with an aluminum hydroxide adjuvant and bred. Ninety-five percent of neonatal mice born to dams immunized with the III- $\alpha$ 2r vaccine survived challenge with GBS expressing type III CPS, and 60% survived challenge with GBS expressing wild-type (nine-repeat) alpha C protein; 18 and 17%, resp., of mice in the neg. control groups survived ( $P$ ,  $<0.0001$ ). These protection levels did not differ significantly from those obtained with the type III CPS-tetanus toxoid conjugate vaccine and the unconjugated two-repeat alpha C protein, which protected 98 and 58% of neonates from infection with GBS expressing type III CPS or the alpha C protein, resp. Thus, the two-repeat alpha C protein in the vaccine was immunogenic and simultaneously enhanced the immunogenicity of type III CPS. III- $\alpha$  vaccines may be alternatives to GBS polysaccharide-tetanus toxoid vaccines, eliciting addnl. antibodies protective against GBS infection.

AN 1999:291215 HCAPLUS <<LOGINID::20081124>>

DN 131:72432

TI Alpha C protein as a carrier for type III capsular polysaccharide and as a protective protein in group B streptococcal vaccines

AU Gravekamp, Claudia; Kasper, Dennis L.; Paoletti, Lawrence C.; Madoff, Lawrence C.

CS Channing Laboratory, Boston, MA, 02115, USA

SO Infection and Immunity (1999), 67(5), 2491-2496

CODEN: INFIBR; ISSN: 0019-9567

PB American Society for Microbiology

DT Journal

LA English

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI A new method of non-crosslinking conjugation of polysaccharides to proteins via thioether bonds for the preparation of saccharide-protein conjugate vaccines

AB Bacterial polysaccharides, including capsular polysaccharides, are poor immunogens particularly in young infants. However, conjugation of bacterial polysaccharides to immunogenic carrier proteins generally results in conjugates that induce strong antipolysaccharide T-helper-cell dependent immune responses, also in young infants. The magnitude of the response and the extent of the T-helper-cell dependency is related to the chemical characteristics of the particular conjugate such as presence or

absence of polysaccharide-protein crosslinking, presence or absence of spacer arms, character of spacer arms, type of carrier protein, size of conjugated polysaccharide hapten and molar degree of substitution. In the present study a new, general and simple method for the preparation of poly- and oligosaccharide-protein conjugates is presented. This new method is based on spacer-introducing chemical that allows for conjugation of a model polysaccharide, dextran, ranging in size from 0.5 to 150 kDa, to tetanus toxoid (TTd). The developed conjugation method involves derivatization of polysaccharide with 2-iminothiolane (2-IT) and activation of carrier protein, such as TTd, with N-hydroxysuccinimide ester of bromoacetic acid. Reaction rates and accordingly the substitution of the conjugates, could be controlled by varying time, pH and concentration of the reactants. Unlike direct reductive amination, the 2-IT based conjugation technol. is fast and made it possible to couple fairly large polysaccharides to TTd.

AN 1999:234182 HCAPLUS <<LOGINID::20081124>>

DN 131:78311

TI A new method of non-crosslinking conjugation of polysaccharides to proteins via thioether bonds for the preparation of saccharide-protein conjugate vaccines

AU Pawlowski, Andrzej; Kallenius, Gunilla; Svenson, Stefan B.

CS Department of Bacteriology, Swedish Institute for Infectious Disease Control, Stockholm, S-105 21, Swed.

SO Vaccine (1999), 17(11-12), 1474-1483

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Multivalent pneumococcal capsular polysaccharide conjugate vaccines employing genetically detoxified pneumolysin as a carrier protein

AB A genetically detoxified pneumolysin, pneumolysoid (PLD), was investigated as a carrier protein for pneumococcal capsular polysaccharide (CPS). Such a CPS-PLD conjugate might provide addnl. protection against pneumococcal infections and resultant tissue damage. A single point mutant of pneumolysin was selected, which lacked measurable hemolytic activity, but exhibited the overall structural and immunol. properties of the wild type. PLD conjugates were prepared from CPS serotypes 6B, 14, 19F, and 23F by reductive amination. The structural features of free PLD, as well as the corresponding CPS-PLD, as assessed by CD spectroscopy, were virtually indistinguishable from the wild type counterpart. Each of the CPS monovalent and tetravalent conjugate formulations were examined for immunogenicity in mice at both 0.5 and 2.0 µg CPS per dose. Tetanus toxoid (TT) conjugates were similarly created and used for comparison. The resultant conjugate vaccines elicited high levels of CPS-specific IgG that was opsonophagocytic for all serotypes tested. Opsonophagocytic titers, expressed as reciprocal dilns. resulting in 50% killing using HL-60 cells, ranged from 100 to 30000, depending on the serotype and formulation. In general, the lower dose and tetravalent formulations yielded the best responses for all serotypes (i.e., either equivalent or better than the higher dose and monovalent formulations). The PLD conjugates were also generally equivalent to or better in CPS-specific responses than the TT conjugates. In particular, both the PLD conjugate and the tetravalent formulations induced responses for type 23F CPS that were approx. an order of magnitude greater than that of the corresponding TT conjugate and monovalent formulations. In addition, all the

PLD conjugates elicited high levels of pneumolysin-specific IgG which were shown to neutralize pneumolysin-induced hemolytic activity in vitro. As a result of these findings, PLD appears to provide an advantageous alternative to conventional carrier proteins for pneumococcal multivalent CPS conjugate vaccines.

AN 1998:644179 HCAPLUS <<LOGINID::20081124>>

DN 130:64887

TI Multivalent pneumococcal capsular polysaccharide conjugate vaccines employing genetically detoxified pneumolysin as a carrier protein

AU Michon, Francis; Fusco, Peter C.; Minetti, Conceicao A. S. A.; Laude-Sharp, Maryline; Uitz, Catherine; Huang, Chun-Hsien; D'Ambra, Anello J.; Moore, Samuel; Remeta, David P.; Heron, Iver; Blake, M. S.

CS North American Vaccine, Inc., Beltsville, MD, 21046, USA

SO Vaccine (1998), 16(18), 1732-1741

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Streptococcus pneumoniae type 14 polysaccharide-conjugate vaccines: length stabilization of opsonophagocytic conformational polysaccharide epitopes

AB A simple and convenient method was developed for the preparation of Streptococcus pneumoniae type 14 polysaccharide (Pn14PS)-tetanus toxoid (TT) conjugate vaccines, using terminally linked Pn14PS fragments of different lengths. Native Pn14PS was simultaneously depolymerized and activated for conjugation by partial N-deacetylation followed by nitrous acid deamination which yielded fragments (1.4 to 150.0 kDa) having a free aldehyde at the reducing end. These were then conjugated to TT through their terminal aldehydic groups, using the reductive amination procedure. All of the above conjugates, when injected in rabbits, induced anti-Pn14PS antibodies, whereas the native Pn14PS did not. The amounts of anti-Pn14PS antibodies elicited by these conjugates, as determined by ELISA, followed a trend with conjugates containing the highest-molecular-weight Pn14PS eliciting the highest titers. The same trend was also observed in the ability of the antibodies to opsonize and kill live type 14 pneumococci, although the increase in opsonophagocytic activity was more pronounced and did not correlate linearly with increases in antibody titer. Competitive inhibition of the binding of different conjugate antisera to the native Pn14PS, using Pn14PS fragments as inhibitors, established that the conjugates induced antibodies with specificities for different lengths of Pn14PS beginning at 2 repeating units (RU). It was also established, both immunologically and antigenically, that at least 4 RU of Pn14PS were required to form an extended conformational epitope and that approx. 22 RU of Pn14PS were required to duplicate the same epitope on the same saccharide chain. The conformational epitope was found to be essential for the induction of antibodies with high opsonophagocytic activity and that augmentation of opsonophagocytic activity was also dependent on further chain extension.

AN 1998:363136 HCAPLUS <<LOGINID::20081124>>

DN 129:121330

OREF 129:24848h,24849a

TI Streptococcus pneumoniae type 14 polysaccharide-conjugate vaccines: length stabilization of opsonophagocytic conformational polysaccharide epitopes

AU Laferriere, Craig A.; Sood, Ramesh K.; De Muys, Jean-Marc; Michon, Francis; Jennings, Harold J.

CS Institute for Biological Sciences, National Research Council of Canada,  
Ottawa, ON, K1A 0R6, Can.

SO Infection and Immunity (1998), 66(6), 2441-2446  
CODEN: INFIBR; ISSN: 0019-9567

PB American Society for Microbiology

DT Journal

LA English

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Structural properties of group B streptococcal type III  
polysaccharide conjugate vaccines that influence immunogenicity  
and efficacy

AB In this study, we tested the hypothesis that the immunogenicity and  
protective efficacy of polysaccharide-protein conjugate vaccines  
are influenced by three variables: (i) mol. size of the conjugate, (ii)  
mol. size of the polysaccharide used for conjugation, and (iii)  
extent of polysaccharide-to-protein crosslinking. Type III  
group B Streptococcus capsular polysaccharide was  
linked by reductive amination at multiple sites to  
tetanus toxoid to create a polysaccharide-protein conjugate  
(III-TT). A single lot of III-TT was fractionated into small, medium, and  
large Mr pools. Whereas all three conferred protection in a maternal  
immunization-neonatal challenge model in mice, the smallest Mr conjugate  
evoked less polysaccharide-specific IgG than the two larger Mr  
conjugates. To test whether the mol. size of the polysaccharide  
used for conjugation also affected the immunogenicity of the conjugate,  
vaccines were synthesized using capsular polysaccharides with  
Mrs of 38,000, 105,000, and 349,000. Polysaccharide-specific  
IgG responses in mice increased with the Mr of the polysaccharides, and  
protective efficacy was lower for the smallest polysaccharide  
conjugate compared to the other two vaccines. Immunogenicity testing of a  
series of vaccines prepared with different degrees of polysaccharide  
-to-protein crosslinking demonstrated higher polysaccharide  
-specific antibody responses as the extent of crosslinking increased.  
However, opsonic activity was greatest in mouse antiserum raised to a  
moderately cross-linked conjugate, suggesting that some antibodies evoked  
by highly cross-linked conjugates were directed to a nonprotective  
epitope. We conclude that conjugate size, polysaccharide size,  
and degree of polysaccharide-protein crosslinking influence the  
immunogenicity and protective efficacy of III-TT conjugate vaccines.

AN 1998:296952 HCAPLUS <<LOGINID::20081124>>

DN 129:53190

OREF 129:11083a

TI Structural properties of group B streptococcal type III  
polysaccharide conjugate vaccines that influence immunogenicity  
and efficacy

AU Wessels, Michael R.; Paoletti, Lawrence C.; Guttormsen, Hilde-Kari;  
Michon, Francis; D'ambra, Anello J.; Kasper, Dennis L.

CS Channing Laboratory, Brigham and Women's Hospital, Boston, MA, 02115, USA

SO Infection and Immunity (1998), 66(5), 2186-2192  
CODEN: INFIBR; ISSN: 0019-9567

PB American Society for Microbiology

DT Journal

LA English

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Meningococcal vaccine development: a novel approach

AB Neisseria meningitidis is a major world-wide cause of meningitis. Effective capsular polysaccharide (CPS) vaccines, that elicit CPS-specific bactericidal (BC) antibodies, were previously developed and licensed to protect against meningococcal disease. However, due to their T-cell independent character, CPS vaccines are useless in infants and do not provide immunol. memory or long-lasting protection in adults. CPS-protein conjugate vaccines are being developed to improve and broaden vaccine efficacy by creating T-cell dependent antigens. However, group B meningococci (GBM) are responsible for nearly half of meningococcal disease and possess a CPS, composed of polysialic acid, that is poorly immunogenic. N-propionyl (NPr) modification of the GBM polysaccharide (GBMP) has enhanced its immunogenicity, but BC antibodies are not induced at high levels, even when conjugated to conventional protein carriers, unless adjuvants stronger than aluminum hydroxide are used. We have chosen to couple the NPr-GBMP by reductive amination to a recombinant GBM class 3 porin (rProB), which we have shown to modulate the immune response in animals towards the production of CPS-specific BC antibodies. We have also combined this conjugate with similar CPS-rProB conjugates for groups A and C meningococci to form a trivalent A/B/C conjugate vaccine. This trivalent meningococcal vaccine has been shown to be safe and highly immunogenic in mice and non human primates, generating CPS-specific BC antibodies for each of the 3 major serogroups, which should provide world-wide protection against meningococcal disease.

AN 1998:97206 HCAPLUS <<LOGINID::20081124>>

DN 128:203874

OREF 128:40311a,40314a

TI Meningococcal vaccine development: a novel approach

AU Fusco, Peter C.; Blake, M. S.; Michon, Francis

CS North American Vaccine, Inc., Beltsville, MD, 20705, USA

SO Expert Opinion on Investigational Drugs (1998), 7(2), 245-252

CODEN: EOIDER; ISSN: 0967-8298

PB Ashley Publications

DT Journal

LA English

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Combination conjugate vaccines against multiple serotypes of group B streptococci

AB Immunity to group B streptococci (GBS) is correlated to the presence of antibodies to the capsular polysaccharides (CPS). Conjugation of type III CPS to the beta C protein results in high IgG titer to both components. Here, the authors have examined the immunogenicity of capsular polysaccharides of four GBS serotypes (Ia, Ib, II, III) after conjugation to the beta C protein by reductive amination.

AN 1998:3712 HCAPLUS <<LOGINID::20081124>>

DN 128:74010

OREF 128:14447a,14450a

TI Combination conjugate vaccines against multiple serotypes of group B streptococci

AU Michon, F.; Fusco, P. C.; D'Ambra, A. J.; Laude-Sharp, M.; Long-Rowe, K.; Blake, S.; Tai, J. Y.

CS North American Vaccine, Inc., Beltsville, MD, USA

SO Advances in Experimental Medicine and Biology (1997), 418(Streptococci and the Host), 847-850

CODEN: AEMBAP; ISSN: 0065-2598

PB Plenum Publishing Corp.

DT Journal

LA English

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI The synthesis of Streptococcus pneumoniae polysaccharide-tetanus  
toxoid conjugates and the effect of chain length on immunogenicity  
AB To study the relationship between length of pneumococcal  
polysaccharide and immunol. performance in rabbits we took well  
defined fragments of the capsular polysaccharides of S.  
pneumoniae types 3, 6A, 18C, 19F and 23F and pneumococcal C-  
polysaccharide and linked them terminally by reductive  
amination to tetanus toxoid. Contrary to other reports we found  
little variation in antibody titers with increasing length. In general  
the opsonophagocytic titers determined using activated HL60 cells and rabbit  
peritoneal cells correlated well with the antibody titers except for that  
of type 3, which despite the presence of high polysaccharide  
antibody titers gave unexpectedly low opsonophagocytic titers. The C-  
polysaccharide-conjugate was also immunogenic when injected in  
both rabbits and mice but gave low opsonophagocytic titers. It was  
demonstrated that opsonophagocytosis was solely dependent on the presence  
of phosphorylcholine-specific antibody and that the induction of these  
antibodies was species dependent.

AN 1997:223134 HCAPLUS <<LOGINID::20081124>>

DN 126:249943

OREF 126:48319a,48322a

TI The synthesis of Streptococcus pneumoniae polysaccharide-tetanus  
toxoid conjugates and the effect of chain length on immunogenicity

AU Laferriere, Craig A.; Sood, Ramesh K.; De Muys, Jean-Marc; Michon,  
Francis; Jennings, Harold J.

CS North American Vaccine Laboratory, National Research Council of Canada,  
Ottawa, ON, Can.

SO Vaccine (1997), 15(2), 179-186

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier

DT Journal

LA English

L14 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Neonatal mouse protection against infection with multiple group B  
streptococcal (GBS) serotypes by maternal immunization with a tetravalent  
GBS polysaccharide-tetanus toxoid conjugate vaccine

AB Most cases of neonatal sepsis and meningitis caused by group B  
streptococci (GBS) are attributable to one of four major capsular  
serotypes: Ia, Ib, II, or III. Because resistance to infection with GBS  
has been correlated with the presence of serum antibodies to the  
type-specific capsular polysaccharides in both exptl. animals  
and human neonates, efforts have been made to elicit protective immunity  
with GBS capsular polysaccharide vaccines. However,  
the GBS capsular polysaccharides alone are not highly  
immunogenic in either animal or human volunteers. Therefore, the authors  
and other investigators have attempted to enhance immunogenicity by  
coupling individual capsular polysaccharides to a carrier  
protein. Here the authors report the synthesis and immunogenicity in  
rabbits of a GBS type Ib polysaccharide-tetanus toxoid vaccine  
prepared by the direct, covalent attachment of tetanus toxoid to a selected  
number of sialic acid residues on the type-specific polysaccharide.  
In addition, the Ib polysaccharide-tetanus toxoid conjugate vaccine  
was combined with similar tetanus toxoid conjugates of GBS type Ia, II,  
and III polysaccharides to form a tetravalent GBS conjugate vaccine.  
Protective efficacy of the GBS tetravalent conjugate vaccine was



demonstrated in a mouse maternal immunization-neonatal challenge model of GBS infection. The results support testing in human subjects of a multivalent GBS conjugate vaccine of this design, with the eventual goal of protecting newborns against GBS infection.

AN 1994:555116 HCAPLUS <<LOGINID::20081124>>

DN 121:155116

OREF 121:28049a,28052a

TI Neonatal mouse protection against infection with multiple group B streptococcal (GBS) serotypes by maternal immunization with a tetravalent GBS polysaccharide-tetanus toxoid conjugate vaccine

AU Paoletti, Lawrence; Wessels, Michael R.; Rodewald, Ariane K.; Shroff, Amy A.; Jennings, Harold J.; Kasper, Dennis L.

CS Channing Laboratory, Brigham and Women's Hospital, Boston, MA, 02115, USA

SO Infection and Immunity (1994), 62(8), 3236-43

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

L14 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Maternal immunization of mice with group B streptococcal type III polysaccharide-beta C protein conjugate elicits protective antibody to multiple serotypes

AB Group B streptococcal infection is major cause of neonatal mortality. Antibody to the capsular polysaccharide protects against invasive neonatal disease, but immunization with capsular polysaccharides fails to elicit protective antibody in many recipients. Conjugation of the polysaccharide to tetanus toxoid has been shown to increase immune response to the polysaccharide. In animal models, C proteins of group B streptococci are also protective determinants. The authors examined the ability of the beta C protein to serve in the dual role of carrier for the polysaccharide and protective immunogen. Type III polysaccharide was covalently coupled to beta C protein by reductive amination. Immunization of rabbits with the polysaccharide-protein conjugate elicited high titers of antibody to both components, and the serum induced opsonophagocytic killing of type III, Ia/C, and Ib/C strains of group B streptococci. Female mice were immunized with the conjugate vaccine and then bred; 93% of neonatal pups born to these dams vaccinated with conjugate survived type III group B streptococcal challenge and 76% survived type Ia/C challenge, compared with 3% and 8% survival, resp., in controls. The beta C protein acted as an effective carrier for the type III polysaccharide while simultaneously inducing protective immunity against beta C protein-containing strains of group B streptococci.

AN 1994:531894 HCAPLUS <<LOGINID::20081124>>

DN 121:131894

OREF 121:23825a,23828a

TI Maternal immunization of mice with group B streptococcal type III polysaccharide-beta C protein conjugate elicits protective antibody to multiple serotypes

AU Madoff, Lawrence C.; Paoletti, Lawrence C.; Tai, Joseph Y.; Kasper, Dennis L.

CS Channing Laboratory, Brigham and Women's Hospital, Boston, MA, 02115, USA

SO Journal of Clinical Investigation (1994), 94(1), 286-92

CODEN: JCINAO; ISSN: 0021-9738

DT Journal

LA English

L14 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Group B Streptococcus type II polysaccharide-tetanus toxoid conjugate vaccine

AB Group B streptococci (GBS) are the most common cause of bacterial sepsis

and meningitis in neonates in the United States. Although the capsular polysaccharide of GBS is an important virulence factor, it is variably immunogenic in humans. The authors increased the immunogenicity of GBS type II polysaccharide by coupling it to tetanus toxoid (TT). Like other GBS capsular polysaccharides, the type II polysaccharide has side chains terminating in sialic acid. Controlled periodate oxidation of native II polysaccharide resulted in the conversion of 7% of sialic acid residues to an analog of sialic acid, 5-acetamido-3,5-dideoxy-D-galactosyloctulosonic acid. TT was conjugated to free aldehyde groups created on the oxidized sialic acid residues by reductive amination. Serum from rabbits vaccinated with type II-TT conjugate (II-TT) vaccine contained antibodies specific to type II polysaccharide as well as to TT, whereas rabbits vaccinated with uncoupled native type II polysaccharide failed to produce a type-specific antibody response. Antibodies elicited by II-TT vaccine were serotype specific and mediated phagocytosis and killing in vitro of type II GBS by human peripheral blood leukocytes. Serum from rabbits vaccinated with II-TT vaccine provided 100% protection in a mouse model of GBS type II infection. Antibodies induced by II-TT vaccine were specific for the native but not desialylated type II polysaccharide, suggesting that an important antigenic epitope of II-TT vaccine was dependent on the presence of sialic acid. Therefore, the coupling strategy which selectively modified a portion of the sialic acid residues of type II polysaccharide before coupling the polysaccharide to TT preserved the epitope essential to protective immunity and enhanced the immunogenicity of the polysaccharide.

AN 1993:78831 HCAPLUS <<LOGINID::20081124>>

DN 118:78831

OREF 118:13815a,13818a

TI Group B Streptococcus type II polysaccharide-tetanus toxoid conjugate vaccine

AU Paoletti, Lawrence C.; Wessels, Michael R.; Michon, Francis; DiFabio, Jose; Jennings, Harold J.; Kasper, Dennis L.

CS Channing Lab., Brigham Women's Hosp., Boston, MA, 02115, USA

SO Infection and Immunity (1992), 60(10), 4009-14

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

L14 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Oligosaccharide conjugate vaccines

AB An improved method is provided for producing oligosaccharide conjugate vaccines. The method comprises (1) reacting an oligosaccharide having a terminal reducing group with diaminoethane in the presence of pyridine borane such that reductive amination occurs; (2) reacting the aminated oligosaccharide with a mol. having 2 functional groups, 1 of which can react with the terminal group of the activated oligosaccharide and the other of which can react with a carrier protein; and (3) reacting the activated oligosaccharide product of 2 with a carrier protein to form a conjugate. The bifunctional mol. is e.g. a diester of adipic acid or of succinic acid. The process of the invention permits the efficient synthesis of glycoconjugates at production rates significantly faster than currently employed methods. Capsular polysaccharide of Streptococcus pneumoniae (e.g. S. pneumoniae type 6A polysaccharide) was hydrolyzed, and the resulting oligosaccharide haptens were treated with diaminomethane, pyridine borane, and then with the succinimidyl diester of succinic (or adipic) acid. The activated oligosaccharides were conjugated to Corynebacterium diphtheriae CRM197 protein, and the immunogenicity of the glycoconjugates was determined. The immune response to the glycoconjugates was monospecific and homogeneous.

AN 1992:253939 HCAPLUS <<LOGINID::20081124>>  
 DN 116:253939  
 OREF 116:43051a,43054a  
 TI Oligosaccharide conjugate vaccines  
 IN Porro, Massimo  
 PA American Cyanamid Co., USA  
 SO Eur. Pat. Appl., 38 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 477508	A1	19920401	EP 1991-113163	19910806 <--
	EP 477508	B1	19950712		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
	US 5153312	A	19921006	US 1990-590649	19900928 <--
	IL 99119	A	19961114	IL 1991-99119	19910807 <--
	JP 06340550	A	19941213	JP 1991-270517	19910924 <--
	JP 3027452	B2	20000404		
	CA 2052323	A1	19920329	CA 1991-2052323	19910926 <--
	CA 2052323	C	20010417		
	FI 9104564	A	19920329	FI 1991-4564	19910927 <--
	FI 104046	B1	19991115		
	HU 58529	A2	19920330	HU 1991-3103	19910927 <--
	HU 211210	B	19951128		
	NO 9103812	A	19920330	NO 1991-3812	19910927 <--
	NO 300759	B1	19970721		
	AU 9184833	A	19920402	AU 1991-84833	19910927 <--
	AU 634663	B2	19930225		
	CN 1060294	A	19920415	CN 1991-109424	19910927 <--
	CN 1034054	C	19970219		
	ZA 9107771	A	19920624	ZA 1991-7771	19910927 <--
	PL 169926	B1	19960930	PL 1991-291855	19910927 <--
	SK 280112	B6	19990806	SK 1991-2969	19910927 <--
	KR 217317	B1	19991001	KR 1991-16912	19910927 <--
	CZ 285650	B6	19991013	CZ 1991-2969	19910927 <--
	US 5306492	A	19940426	US 1992-921678	19920730 <--
PRAI	US 1990-590649	A	19900928	<--	

L14 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI An oligosaccharide-tetanus toxoid conjugate vaccine against type III group B Streptococcus

AB An oligosaccharide-tetanus toxoid conjugate vaccine was developed against type III group B Streptococcus. Purified group B streptococcal type III capsular polysaccharide was depolymd. by enzymic digestion using endo- $\beta$ -galactosidase produced by Citrobacter freundii. Following enzymic digestion, oligosaccharides were fractionated by gel filtration chromatog. on Sephadex G-75. An oligosaccharide pool of average mol. weight 14,500 (corresponding to 13.6 repeating units of the type

III polysaccharide) was used for conjugation to tetanus toxoid. Tetanus toxoid was covalently coupled via a synthetic spacer mol. to the reducing end of the oligosaccharide by reductive amination. The oligosaccharide-tetanus toxoid conjugate elicited type III-specific anticapsular antibodies (measured in ELISA) in 3 out of 3 rabbits whereas the unconjugated native type III polysaccharide was nonimmunogenic. Antiserum from rabbits vaccinated with the oligosaccharide-protein conjugate protected mice against lethal challenge with live group B streptococci (16 out of 16 mice survived) and opsonized group B streptococci for phagocytosis in vitro. No protection was

conferred by preimmune serum nor by serum from rabbits vaccinated with unconjugated native type III polysaccharide. An oligosaccharide-protein conjugate vaccine of this design may prove to be an effective immunogen for protection against group B streptococcal infection in humans. In addition, the approach to vaccine design utilized in these studies will facilitate further definition of the structural parameters that determine immune response to glycoconjugate vaccines.

AN 1991:4512 HCAPLUS <<LOGINID::20081124>>

DN 114:4512

OREF 114:911a,914a

TI An oligosaccharide-tetanus toxoid conjugate vaccine against type III group B Streptococcus

AU Paoletti, Lawrence C.; Kasper, Dennis L.; Michon, Francis; DiFabio, Jose; Holme, Kevin; Jennings, Harold J.; Wessels, Michael R.

CS Channing Lab., Brigham and Women's Hosp., Boston, MA, 02115, USA

SO Journal of Biological Chemistry (1990), 265(30), 18278-83  
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

L14 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Immunogenicity in animals of a polysaccharide-protein conjugate vaccine against type III group B Streptococcus

AB The native capsular polysaccharide of type III group B Streptococcus elicits a specific antibody response in only 60% of nonimmune human subjects. To enhance the immunogenicity of this polysaccharide, the type III polysaccharide was coupled to tetanus toxoid. Prior to coupling, aldehyde groups were introduced on the polysaccharide by controlled periodate oxidation, resulting in the conversion of 25% of the sialic acid residues of the polysaccharide to residues of the 8-carbon analog of sialic acid, 5-acetamido-3,5-dideoxy-D-galactosyloctulosonic acid. Tetanus toxoid was conjugated to the polysaccharide by reductive amination, via the free aldehyde groups present on the partially oxidized sialic acid residues. Rabbits vaccinated with the conjugate vaccine produced IgG antibodies that reacted with the native type III group B streptococcal polysaccharide, while rabbits immunized with the unconjugated type III polysaccharide failed to respond. Sera from animals receiving conjugate vaccine opsonized type III group B streptococci for phagocytic killing by human peripheral blood leukocytes, and protected mice against lethal challenge with live type III group B streptococci. The results suggest that this method of conjugation to a carrier protein may be a useful strategy to improve the immunogenicity of the type III group B Streptococcus polysaccharide in human subjects.

AN 1990:629149 HCAPLUS <<LOGINID::20081124>>

DN 113:229149

OREF 113:38645a,38648a

TI Immunogenicity in animals of a polysaccharide-protein conjugate vaccine against type III group B Streptococcus

AU Wessels, Michael R.; Paoletti, Lawrence C.; Kasper, Dennis L.; DiFabio, Jose L.; Michon, Francis; Holme, Kevin; Jennings, Harold J.

CS Channing Lab., Brigham and Women's Hosp., Boston, MA, 02115, USA

SO Journal of Clinical Investigation (1990), 86(5), 1428-33  
CODEN: JCINAO; ISSN: 0021-9738

DT Journal

LA English

L14 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI GLC-MS of N-(1-deoxyalditol-1-yl)octadecylamine derivatives in the analysis of methanolysates of neoglycolipids obtained by reductive

amination

AB Hydrophobic conjugates of a series of aldoses have been prepared by reductive amination with octadecylamine and sodium cyanoborohydride, as model compds. for the anal. of reductively aminated oligosaccharides derived from capsular polysaccharides of *Streptococcus pneumoniae*. In the context of the methanolysis procedure for sugar anal., GLC and GLC-MS studies were carried out on the N-(1-deoxyalditol-1-yl)octadecylamine derivs. obtained after treatment with methanolic HCl, and subsequent N-acetylation and trimethylsilylation.

AN 1989:420786 HCAPLUS <<LOGINID::20081124>>

DN 111:20786

OREF 111:3590h,3591a

TI GLC-MS of N-(1-deoxyalditol-1-yl)octadecylamine derivatives in the analysis of methanolysates of neoglycolipids obtained by reductive amination

AU Van Dam, Jan E. G.; Maas, Augustinus A. M.; Kamerling, Johannes P.; Vliegenthart, Johannes, F. G.

CS Dep. Bio-Org. Chem., Utrecht Univ., Utrecht, NL-3508 TB, Neth.

SO Carbohydrate Research (1989), 187(1), 25-34

CODEN: CRBRAT; ISSN: 0008-6215

DT Journal

LA English

L14 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Immunogenic conjugates comprising the reductive amination product of bacterial polysaccharide capsule fragments and bacterial toxins or toxoids, especially for human infants

AB Immunogenic conjugates are the reductive amination products of an immunogenic bacterial capsule fragments and a bacterial toxin or toxoid. The conjugates are prepared and used as vaccines for young mammals, including humans, especially infants. The capsular polymer fragment prior to conjugation has  $\geq 1$  aldehyde group at each end of the fragment; the final conjugate made with the capsular polymers has a lattice or network structure, and provides extremely high levels of anticapsular polymer antibodies in infants. The capsular polymer of *Haemophilus influenzae* type b (PRP) Na salt was cleaved with acid and fragments containing 15-34 ribose units were treated with CRM197 (diphtheria toxin analog) in the presence of NaBH<sub>3</sub>CN to give the PRP-CRM197 conjugate (I) as a multimol. aggregate. In infants from 12-27 mo, the injection of I led to enhanced formation of anti-PRP antibodies as well as antidiphtheria toxoid antibodies.

AN 1988:156458 HCAPLUS <<LOGINID::20081124>>

DN 108:156458

OREF 108:25600h,25601a

TI Immunogenic conjugates comprising the reductive amination product of bacterial polysaccharide capsule fragments and bacterial toxins or toxoids, especially for human infants

IN Anderson, Porter W.; Eby, Ronald John

PA Praxis Biologics, Inc., USA

SO Eur. Pat. Appl., 58 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 245045	A2	19871111	EP 1987-303928	19870501 <--
	EP 245045	A3	19890426		
	EP 245045	B1	19931103		
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
	US 4902506	A	19900220	US 1986-859975	19860505 <--

CA 1276109	C	19901113	CA 1987-536090	19870430 <--
WO 8706838	A1	19871119	WO 1987-US1020	19870501 <--
W: AU, DK, JP				
AU 8773935	A	19871201	AU 1987-73935	19870501 <--
AU 601742	B2	19900920		
JP 01500036	T	19890112	JP 1987-502838	19870501 <--
JP 2559438	B2	19961204		
AT 96676	T	19931115	AT 1987-303928	19870501 <--
ES 2059372	T3	19941116	ES 1987-303928	19870501 <--
JP 08283282	A	19961029	JP 1996-22882	19870501 <--
DK 8800025	A	19880105	DK 1988-25	19880105 <--
DK 175489	B1	20041108		
PRAI US 1986-859975	A	19860505	<--	
US 1981-298102	B2	19810831	<--	
US 1983-511048	A2	19830705	<--	
EP 1987-303928	A	19870501	<--	
JP 1987-502838	A3	19870501	<--	
WO 1987-US1020	A	19870501	<--	

L14 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Immunogenic conjugates for vaccines against childhood diseases.

AB An immunogenic conjugate comprises the reductive amination product of an immunogenic capsular polymer fragment of 10-30 monomeric units and a reducing end. The fragment is derived from the capsular polymer of a Streptococcus pneumoniae or Haemophilus influenzae bacterium and a bacterial toxin or toxoid. A vaccine containing the conjugates allows active immunization of young mammals against systemic bacterial infections. An immunogenic conjugate comprising diphtheria toxin protein CRM197 and H. influenzae capsular polysaccharide PRPvs fragment (preparation given) was used to immunize children of age 1-2 yr via s.c. injection of a vaccine containing 25mg conjugate in saline (2-3 vaccinations at ≥1 mo. intervals). No toxic reactions were observed, and higher antibody titers were observed with the CRM carrier than without and with secondary vaccination.

AN 1987:561671 HCAPLUS <<LOGINID::20081124>>

DN 107:161671

OREF 107:25889a,25892a

TI Immunogenic conjugates for vaccines against childhood diseases.

IN Anderson, Porter W.

PA USA

SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 298,102, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 4673574	A	19870616	US 1983-511048	19830705 <--
	US 4808700	A	19890228	US 1984-639293	19840810 <--
	US 4762713	A	19880809	US 1985-732200	19850508 <--
	US 4761283	A	19880802	US 1986-845731	19860328 <--
	US 4902506	A	19900220	US 1986-859975	19860505 <--
	US 5097020	A	19920317	US 1989-423081	19891018 <--
	US 5360897	A	19941101	US 1992-819305	19920109 <--
PRAI	US 1981-298102	A2	19810831	<--	
	US 1983-511048	A2	19830705	<--	
	US 1984-628873	A2	19840709	<--	
	US 1986-859975	A1	19860505	<--	
	US 1989-423081	A1	19891018	<--	

L14 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Immunogens consisting of oligosaccharides from the capsule of *Haemophilus influenzae* type b coupled to diphtheria toxoid or the toxin protein CRM197

AB *H. influenzae* Type b (Hib) capsular polysaccharide (PRP) was selectively hydrolyzed to reducing oligosaccharides, and the fraction containing 3-10 ribosylribitolphosphate repeating units (VS) was conjugated by reductive amination to diphtheria toxin (DTx), its nontoxic derivative CRM197 (Dcr), or diphtheria toxoid (DTd). Conjugate DTx-VS retained .apprx.1% of native toxicity, which was eliminated by treatment with formalin. Immunization of rabbits with the conjugates elicited antibody (Ab) to PRP and to DTx but not to a model for the linkage determinant. Human adults given single s.c. injections had increases in serum Ab to PRP and in bactericidal activity in vitro; the Ab protected infant rats challenged with Hib. Adults had increases also in Ab to DTd, and these Ab protected rabbits against DTx. A series of 2 injections of the conjugates Dcr-VS and DTd-VS was tested in infants beginning at 19-23 mo of age. Rises in anti-PRP Ab after the primary resembled the rises after PRP vaccine. In contrast to PRP, the conjugates elicited large rises after the secondary vaccinations and a substantial IgG component. Development of bactericidal activity paralleled the rises in anti-PRP Ab. Secondary rises after Dcr-VS were higher than after DTd-VS. In infants 12-16 mo of age, Dcr-VS (but not DTd-VS) elicited strong primary and secondary Ab responses that included IgG and bactericidal activity. Both conjugates produced consistent rises in Ab to DTd.

AN 1985:486144 HCAPLUS <<LOGINID::20081124>>

DN 103:86144

OREF 103:13833a,13836a

TI Immunogens consisting of oligosaccharides from the capsule of *Haemophilus influenzae* type b coupled to diphtheria toxoid or the toxin protein CRM197

AU Anderson, Porter; Pichichero, Micael E.; Insel, Richard A.

CS Med. Cent., Univ. Rochester, Rochester, NY, 14642, USA

SO Journal of Clinical Investigation (1985), 76(1), 52-9

CODEN: JCINAO; ISSN: 0021-9738

DT Journal

LA English

L14 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Studies on vaccine control and immunogenicity of polysaccharides of *Streptococcus pneumoniae*

AB An immunoelectrophoretic method was devised for quantitation of 14 polysaccharide components in pneumococcal vaccine and for determination of their stability in the final container. The individual polysaccharide types, 1, 2, 3, 4, 6A, 8, 9N, 12F, 18C, 19F, 23F, and 25 (Danish nomenclature), were present at 80-123% of the labeled concns. Pneumococcal polysaccharide types 3, 6A, 9N, and 19F, used as representative types, were heated at 37° for 24 h and stored at 4°. The concns. of these polysaccharides remained constant over a 12-mo. period, and the mol. sizes of types 3 and 9N were stable during storage. In contrast, the mol. sizes of types 6A and 1.F declined gradually during storage. Pneumococcal type 19F polysaccharide was conjugated to various proteins, i.e., bovine serum albumin, human Ig, and pneumococcal R61 cell wall protein, by reductive amination. Immunization of mice with 19F polysaccharide-protein conjugates increased formation of antibody. Young mice exposed to pneumococcal type 19F polysaccharide-protein conjugate during gestation and suckling had a greater antibody response than did mice that received no type 19F polysaccharide-protein conjugate while suckling or received the conjugate only when they were 2 wk old.

AN 1981:538439 HCAPLUS <<LOGINID::20081124>>

DN 95:138439

OREF 95:23086h,23087a

TI Studies on vaccine control and immunogenicity of polysaccharides of *Streptococcus pneumoniae*

AU Lee, Chi-Jen; Lin, Kuei-Tang

CS Div. Bacterial Prod., Food and Drug Adm., Bethesda, MD, USA

SO Reviews of Infectious Diseases (1981), 3(Suppl.), 51-60

CODEN: RINDDG; ISSN: 0162-0886

DT Journal

LA English

L14 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation and immunological uses of radio-iodinated oligosaccharide derivatives. I. Preparation of iodine-125-labeled oligosaccharide derivatives with the aid of 3-(4-hydroxyphenyl)propionic acid N-hydroxysuccinimide ester

AB 125I-labeled oligosaccharides were prepared by combining acylation and iodination in a 1-step procedure by successive addition of the ester, 3-(4-hydroxyphenyl)propionic acid N-hydroxysuccinimide ester (I), and 125I--chloramine T to the aminoalditol formed by reductive amination of the oligosaccharide. Thus, the oligosaccharide, NaCNBH<sub>3</sub>, and NH<sub>4</sub>OAc in MeOH-H<sub>2</sub>O (2:1) were refluxed for 6 h or stirred at 37° for 6 days; the resulting 1-amino-1-deoxy alditol was separated by high-voltage electrophoresis with .apprx.30% yield of theor. A solution of I and the aminoalditol in borate buffer, pH 8.5 was kept at 0° for 15 min, then carrier-free Na<sup>125</sup>I solution was added, followed by chloramine T in H<sub>2</sub>O (at room temperature). After 5 min the reaction was terminated by

addition of

Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> followed by chromatog. on Sephadex G 25 or Dowex AG 1 + 2, Cl- form. The efficiency of radioiodination was 30%-75%, depending on the compound. The immunoreactivity of the derivs. was assessed by using equilibrium dialysis and the Farr assay. 125I-labeled derivs. were prepared from isomaltotetraose,  $\alpha$ -nigerosyl-1,3-nigerose, and the monomeric and dimeric repeating units of *Klebsiella pneumoniae* capsular polysaccharide. Derivs. of the 1st 2 compds. listed were virtually carrier-free with an extremely high sp. activity of .apprx.2 mCi/ $\mu$ g.

AN 1977:167377 HCAPLUS <<LOGINID::20081124>>

DN 86:167377

OREF 86:26281a,26284a

TI Preparation and immunological uses of radio-iodinated oligosaccharide derivatives. I. Preparation of iodine-125-labeled oligosaccharide derivatives with the aid of 3-(4-hydroxyphenyl)propionic acid N-hydroxysuccinimide ester

AU Himmelspach, K.; Geyer, H.; Hoyer, G.; Schepers, G.

CS Max-Planck-Inst. Immunbiol., Freiburg/Br., Fed. Rep. Ger.

SO FEBS Letters (1977), 75(1), 154-8

CODEN: FEBLAL; ISSN: 0014-5793

DT Journal

LA English